Applicant: Yoshida et al. Attorney's Docket No.: 20214-0002US1

Serial No.: 10/561,298 Filed : June 7, 2006

Page : 2 of 7

## Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

## **Listing of Claims**

1. (Original) A compound represented by formula (1)

$$R_{42}$$
 $R_{42}$ 
 $R_{41}$ 
 $R_{11}$ 
 $R_{31}$ 
 $R_{21}$ 
 $R_{22}$ 
 $R_{23}$ 
 $R_{23}$ 
 $R_{23}$ 
 $R_{23}$ 
 $R_{23}$ 

wherein

R<sub>11</sub>, R<sub>21</sub>, R<sub>31</sub>, and R<sub>41</sub> independently represent a hydrogen or methyl group;

R<sub>22</sub>, R<sub>23</sub>, R<sub>32</sub>, R<sub>33</sub>, R<sub>42</sub>, and R<sub>43</sub> independently represent any one of hydrogen, a linear alkyl group comprising 1 to 6 carbons, a linear alkyl group comprising 1 to 6 carbons to which a nonaromatic cyclic alkyl group or a substituted or unsubstituted aromatic ring is attached, a nonaromatic cyclic alkyl group, or a non-aromatic cyclic alkyl group to which a non-aromatic cyclic alkyl group or a substituted or unsubstituted aromatic ring is attached;

R<sub>21</sub> and R<sub>22</sub>, R<sub>22</sub> and R<sub>23</sub>, R<sub>31</sub> and R<sub>32</sub>, R<sub>32</sub> and R<sub>33</sub>, R<sub>41</sub> and R<sub>42</sub>, and R<sub>42</sub> and R<sub>43</sub> may independently represent a non-cyclic structure without bonding to each other, or may independently represent a cyclic structure by bonding to each other through a linear alkylene group having a chain length of 1 to 5 carbons, a linear alkylene chain having a chain length of 1 to 5 carbons and carrying a branched chain of 1 to 6 carbon atoms, or a linear alkylene chain having a chain length of 1 to 5 carbons and carrying a cyclic structure of 1 to 6 carbon atoms; n can be selected from a range of numbers that enable the compound to have HDAC inhibitory activity; and

Applicant: Yoshida et al. Serial No.: 10/561,298 Filed: June 7, 2006

Page : 3 of 7

X represents a structural component having a structure that can coordinate with the zinc positioned at the active center of histone deacetylase.

2. (Original) The compound of claim 1, wherein X is any one of the substituents represented by the following structural formulas:

OPD

Attorney's Docket No.: 20214-0002US1

Applicant: Yoshida et al. Serial No.: 10/561,298 Filed : June 7, 2006

Page : 4 of 7

- 3. (Original) A histone deacetylase inhibitor comprising the compound of claim 1 as an active ingredient.
- 4. (Original) A tubulin deacetylase inhibitor comprising the compound of claim 1 as an active ingredient.
- 5. (Original) An apoptosis inducer comprising the compound of claim 1 as an active ingredient.
- 6. (Original) A differentiation inducer comprising the compound of claim 1 as an active ingredient.
- (Original) An angiogenesis inhibitor comprising the compound of claim 1 as an active 7. ingredient.
- 8. (Original) A cancer metastasis inhibitor comprising the compound of claim 1 as an active ingredient.

Attorney's Docket No.: 20214-0002US1

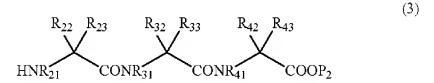
Applicant: Yoshida et al. Serial No.: 10/561,298 Filed: June 7, 2006

Page : 5 of 7

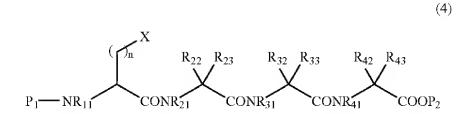
- 9. (Currently Amended) A pharmaceutical agent for treatment or prevention of a disease caused by histone deacetylase, wherein the agent which comprises the compound of claim 1 as an active ingredient.
- 10. (Cancelled)
- 11. (Withdrawn) A method for producing the compound of claim 1, wherein the method comprises reacting a compound represented by formula (2)

$$P_{1} \longrightarrow NR_{11} \qquad COOH \qquad (2)$$

(wherein n, R<sub>11</sub>, and X are as defined in claims 1 and 2, and P<sub>1</sub> represents an amino protecting group) with a compound represented by formula (3)



(wherein R<sub>11</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, R<sub>31</sub>, R<sub>32</sub>, R<sub>33</sub>, R<sub>41</sub>, R<sub>42</sub>, and R<sub>43</sub> are as defined in formula (1) of claim 1, and P<sub>2</sub> represents a carboxyl protecting group) in the presence of a peptide coupling agent to yield a compound represented by formula (4)

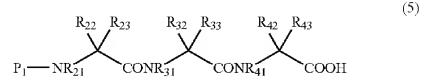


(wherein n, R<sub>11</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, R<sub>31</sub>, R<sub>32</sub>, R<sub>33</sub>, R<sub>41</sub>, R<sub>42</sub>, R<sub>43</sub>, P<sub>1</sub>, P<sub>2</sub>, and X are defined above), then subjecting the compound represented by formula (4) to catalytic hydrogenation, acid treatment, or hydrolysis to remove P<sub>1</sub> and P<sub>2</sub>, and subsequently, carrying out a cyclization reaction in the presence of a peptide coupling agent;

Applicant: Yoshida et al. Attorney's Docket No.: 20214-0002US1

Serial No.: 10/561,298 Filed: June 7, 2006 Page: 6 of 7

reacting a compound represented by formula (5)



(wherein  $R_{21}$ ,  $R_{22}$ ,  $R_{23}$ ,  $R_{31}$ ,  $R_{32}$ ,  $R_{33}$ ,  $R_{41}$ ,  $R_{42}$ ,  $R_{43}$ , and  $P_1$  are as defined above) with a compound represented by formula (6)

$$\begin{array}{c} X \\ \text{HR}_{11} N \\ \end{array} \begin{array}{c} \text{COOP}_2 \end{array}$$

(wherein n,  $R_{11}$ ,  $P_2$ , and X are as defined above) in the presence of a peptide coupling agent to yield a compound represented by formula (7)

(wherein n, R<sub>11</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, R<sub>31</sub>, R<sub>32</sub>, R<sub>33</sub>, R<sub>41</sub>, R<sub>42</sub>, R<sub>43</sub>, P<sub>1</sub>, P<sub>2</sub>, and X are as defined above), then subjecting the compound represented by formula (7) to catalytic hydrogenation, acid treatment, fluoride anion treatment, or hydrolysis to remove P<sub>1</sub> and P<sub>2</sub>, and subsequently, carrying out a cyclization reaction in the presence of a peptide coupling agent; or

reacting a compound in which X of the cyclic tetrapeptide of formula (1) is a carboxyl group or a sulfhydryl group individually with trifluoroacetic anhydride, pentafluoropropanoic anhydride, or 1,1,1-trifluoro-3-bromoacetone to change substituent X into a different type of substituent.